

EXERCISE: SCIENTIFIC RATIONALE

Exercise and the Elderly: A Scientific Rationale for Exercise Prescription

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Abstract

- **Objective:** To review the benefits of exercise intervention in older persons and the role of exercise in the prevention and treatment of chronic disease.
- **Methods:** Qualitative assessment of the literature focusing on randomized controlled trials.
- **Results:** Participation in regular physical activity, including aerobic exercise and strength training, can improve health, functional ability, and quality of life in older persons. Higher levels of aerobic activity are associated with increased physical fitness, decreased total mortality, and improvements in cardiovascular risk profile. Resistance training combats myopathy and osteopenia and increases muscle endurance and function. Additional benefits from exercise include improved bone health and improved postural stability. Starting an exercise program in later life can significantly modify risk factors for morbidity and mortality even if a person has been sedentary in prior years.
- **Conclusion:** Physical activity should be encouraged in healthy seniors and should be considered a primary or adjunctive therapy in the treatment of chronic diseases associated with aging. Physicians can play a major role in communicating the benefits of exercise and encouraging physical activity in their patients.

By the year 2030, the number of individuals aged 65 years and older will reach 70 million in the United States, with persons aged 85 and older constituting the fastest growing segment of the population [1]. This group also represents the population with the highest rate of physical inactivity. Only 30% of those aged 65 and older report any regular exercise. By age 75, about 1 in 3 men and 1 in 2 women do not engage in any physical activity [2]. This inactivity is associated with a greater disease burden and decreased functional status.

Exercise, including aerobic activities and strength training, can improve health, functional ability, and quality of life in older persons, even in the presence of frailty and chronic illness [3]. Higher levels of aerobic activity are associated

with increased physical fitness, decreased total mortality, and improvements in cardiovascular risk profile [4–8]. Resistance training combats myopathy and osteopenia and increases muscle endurance and function [9–12]. Tai chi, yoga, stretching, and balance training may improve physical functioning and may be of benefit in patients with hypertension, heart disease, and arthritis [13–22]. Further, starting an exercise program later in life can significantly modify risk factors for morbidity and mortality even if a person has been sedentary in prior years [23]. As shown in the **Figure**, older women who remained or became active had dramatically lower cardiovascular and all-cause mortality as compared with inactive women over the course of a 5.7-year prospective cohort study ($n = 7553$) [23].

In addition to improving health, exercise also has the potential to reduce health care costs. An analysis of the economic burden of inactivity concluded that physical activity confers a mean net annual benefit of \$330 per person in direct medical expenses [24]. Increasing participation in regular moderate physical activity among the more than 88 million inactive Americans over age 15 could reduce annual national medical costs by as much as \$76.6 billion. Importantly, researchers conclude that the benefits of long-term exercise are not age-specific and are evident even when complicated by multiple chronic diseases.

This article reviews the health benefits of physical activity and exercise, focusing on randomized controlled trials (RCTs) that address exercise in the elderly. Evidence from large prospective cohort studies, meta-analyses, and substantive review articles by experts in the field also is presented. In this article, we review the relevant literature pertaining to the role of exercise in cardiovascular health, strength, postural stability, cognitive function, psychological health, and immune function as well as the prevention and treatment of chronic disease. In a companion article, “Exercise and the elderly: guidelines and practical prescription applications for the clinician” (pp. 117–127), we provide resources and recommendations for prescribing exercise through the use of case studies. It is important for physicians and other health care providers

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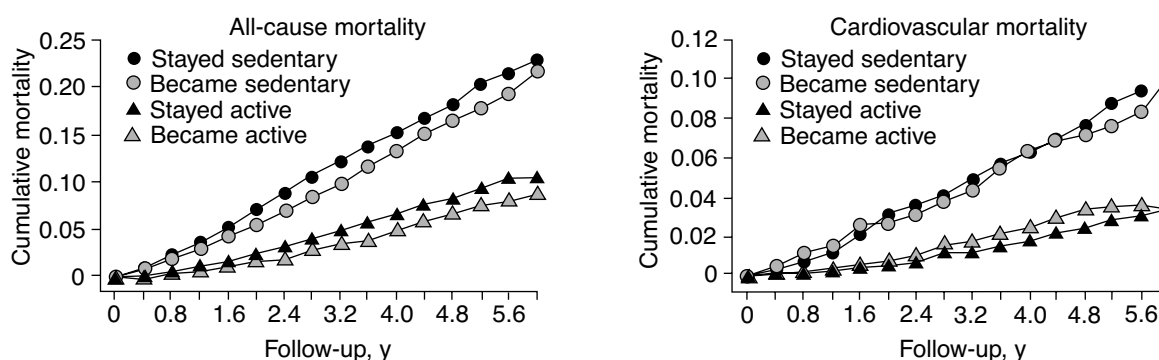


Figure. Relationship of changes in physical activity and mortality among older women. (Reprinted with permission from Gregg EW, Cauley JA, Stone K, et al. Relationship of changes in physical activity and mortality among older women. *JAMA* 2003;289:2379–86.)

to play a major role in disseminating research results, encouraging physical activity, and dispelling myths that persist as barriers to exercise in the elderly.

Benefit of Exercise in Various Health Domains

Cardiovascular Health

Many large cohort studies and several RCTs suggest that regular physical activity and cardiovascular fitness are associated with a reduced risk of coronary heart disease (CHD) [5,25–27]. In a Finnish cohort of 1166 men (aged 42–60), subjects in the highest physical activity tertile had one third the risk of myocardial infarction (MI) as compared with subjects in the lowest tertile [28]. Cardiorespiratory fitness as measured by maximal oxygen uptake (VO_2max) had a strong inverse association with the risk of acute MI. In another study (RCT, $n = 19$), 4 weeks of short bouts of high-intensity endurance exercise (bicycle ergometer, 80% VO_2max , 10 min/session, 6×/day) improved endothelium-dependent vasodilation in both epicardial coronary and resistance vessels in patients with coronary artery disease, indicating a rapid beneficial effect [6]. In addition to total physical activity, running, walking, and weight training were associated with reduced CHD risk in a cohort of 44,452 American men [8].

Lipid and lipoprotein profiles are positively impacted by exercise, even with minimal weight change [7]. Lipoprotein profile improvements appear to be related to the amount of activity, not necessarily exercise intensity or improvement in fitness level. Aerobic exercise has been found to lower serum low-density lipoprotein (LDL) cholesterol in men and postmenopausal women, especially in combination with a diet moderately low in fat and cholesterol [29]. While low amounts of exercise are associated with beneficial changes in plasma lipoprotein profiles, higher levels result in more pronounced changes, with improved high-density lipoprotein (HDL) cholesterol levels [30]. The mechanism behind this effect may include increased lipoprotein lipase activity in adipose tissue

and muscle and/or decreased hepatic lipase and cholesteryl ester transfer protein activity. Enhanced clearance of very low density lipoproteins and chylomicron remnants results in decreased triglyceride exchange availability, increased LDL particle size, and increased HDL cholesterol levels.

Strength

Sarcopenia is the loss of muscle mass and strength that occurs with aging, even in the absence of illness or chronic disease [31]. Often, sarcopenia is accompanied by increased total and central adiposity [32], increasing the risk of cardiovascular complications and other chronic diseases. Longitudinal studies indicate a decline in lean mass of 0.25–0.30 kg/year after age 20, with losses accelerated by advancing age, disease, and menopause [33–35]. Type II muscle fibers, the fast twitch fibers responsible for short, quick movements [36], appear to be primarily affected by this loss, leading to disability, frailty, loss of independence, reduced protein stores to overcome the stress of illness, and increased mortality [37]. Peak skeletal muscle power (force \times velocity of muscle shortening), a strong predictor of functional status and mobility in older people, also has been shown to decline with advancing age, often earlier and more dramatically than loss of strength [38–40]. This loss of power impairs the ability to perform rapid, intense movements, such as the movements needed to reverse a forward fall.

Through high-velocity (rapid, high-power) strength training programs, older men and women have been able to improve muscle power [41,42]. Progressive resistance training (PRT) has been shown to increase both strength and muscle mass at any age and is of benefit even in the presence of underlying disease [37]. Home-, hospital- and/or community-based PRT exercise, when performed properly offers numerous beneficial side effects, including potential improvements in balance, gait stability, sleep quality, mental health, immune function, and overall physical functioning

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[43–47]. In contrast to resistance exercise, aerobic training is less effective in the treatment of age-related sarcopenia [48].

Research indicates that the aging musculoskeletal system retains its responsiveness to PRT [37]. An RCT in 100 frail, very elderly people (aged 72–98) demonstrated that a high-intensity, progressive program (80% of 1-repetition maximum [1-RM], 45 min/session, 3×/week for 10 weeks) can improve muscle strength and size, increase mobility, and lead to higher levels of spontaneous physical activity [48]. While only modest muscle area changes were observed in this population, significant improvements in muscle strength indicate that 10 weeks of PRT can improve neuronal recruitment of existing underused skeletal muscle. Notably, these subjects were older than the average U.S. nursing home resident (mean age, 87), and the protocol did not exclude subjects with chronic disease, unless acutely decompensated or terminal. PRT programs of low intensity/more repetitions (50% 1-RM, 13 repetitions) have proven to be as effective as high-intensity programs (80% 1-RM, 8 repetitions) in improving muscle strength and endurance in adults aged 60 to 83 [49].

Postural Stability

In the population aged 65 and older, falls are the most common cause of nonfatal injuries and trauma-related hospital admissions [50]. Falls are associated with considerable morbidity, mortality, reduced functioning, and premature nursing home admissions in both men and women [51]. Home- and community-based exercise programs have been shown to be feasible and effective in maintaining functional status, improving balance, reducing falls, and lowering the incidence of vertebral fractures [52–59]. In an RCT ($n = 233$), Campbell et al demonstrated that moderate-intensity strengthening and balance exercises coupled with a walking plan, when administered by a physical therapist, decreased falls by 42% and decreased fall-related injuries by 13% in a group of women aged 80 and over [60]. The same home-based exercise program, when administered by a trained nurse, was able to reduce falls by 46% in men and women aged 75 and older ($n = 450$) [61]. Serious injuries and hospital admissions due to falls were reduced, and the program was shown to be cost-effective, especially for those aged 80 years and older. A group-based exercise intervention alone or in combination with home hazard management and vision improvement was found to reduce falls in healthy seniors aged 70 to 84 (RCT, $n = 1090$) [62]. The combination of all 3 interventions resulted in further benefit, decreasing fall rate an estimated 14%, an effect mainly attributed to improvements in balance. Van Haastregt and colleagues provide practical guidelines for health professionals concerned with fall prevention in the elderly [63].

Cognition and Mental Health

Cross-sectional studies suggest that aerobic exercise may pre-

serve and improve cognitive functioning [64]. In a cohort of 349 healthy adults aged 55 and older, high cardiorespiratory fitness was associated with increased preservation of cognitive function over a 6-year period [65]. In an RCT ($n = 36$) in which older exercisers (aged 65–74) followed a 10-week program of aquatic exercise (45 min/session, 3×/week), the exercisers demonstrated substantial improvement on 2 measures of dual-task attention compared with age-matched controls [66]. Walking has been found to improve executive control functions including planning, scheduling, working memory, and inhibition in adults aged 60 to 75 [67]. Most studies indicate that multiple aspects of attention and mental function can be positively affected by aerobic exercise. While leisure time physical activity was not shown to be any more effective than cognitive leisure activities (reading, playing board games) in preventing Alzheimer's disease or dementia in a cohort of 469 adults aged over 75 [68], longitudinal studies suggest that continued physical activity remains an important protective factor against cognitive decline in the elderly [69].

Observational and intervention studies suggest that regular physical exercise reduces symptoms of depression [70]. In an RCT of 156 men and women (aged ≥ 50) with major depressive disorder, a program of aerobic exercise (continuous walking or jogging, 70% to 85% maximal heart reserve, 30 min/session, 3×/week) was found to be as effective as antidepressant medication (sertraline) as measured by both a clinical rating scale and self-reported questionnaire [71]. Observational cohort studies suggest that exercise-based cardiac rehabilitation may improve behavioral and quality-of-life parameters in depressed patients after major cardiac events [72,73]. Although antidepressants may facilitate a more rapid initial therapeutic response, exercise appears equally effective in reducing depression in certain elderly populations.

Strength training also has been shown to modify symptoms of depression. Twenty weeks of unsupervised weight lifting was found to exert an antidepressive effect in depressed elderly patients (mean age, 71; $n = 32$) [46]. One third of these exercisers reported weight lifting regularly at a 26-week follow-up, suggesting that long-term changes in exercise behavior are possible in some subjects, even without supervision. Ten weeks of supervised weight training was shown in an RCT ($n = 32$) to improve subjective sleep quantity and quality in subjects aged 60 to 84 with major or minor depression or dysthymia [74].

Immune Function

While aging is associated with declines in immune function, especially T cell-dependent functions [75], exercise may slow or prevent the age-related decline in immune response. Cross-sectional comparisons have found that highly conditioned elderly women have superior natural killer cell activity and

T cell function when compared with age-matched sedentary controls [76]. Intervention studies have returned contradictory findings, suggesting that other factors, such as the duration of physical activity and baseline health status, may play a more central role in immune outcomes. While moderate exercise in healthy or arthritic elderly has never been shown to harm immune parameters, many researchers show no effect of aerobic or resistance training on immune markers such as cytokine production, prostaglandin E_2 production, serum cortisol, lymphocyte subsets, lymphocyte proliferation, natural killer cell-mediated cytotoxicity, or delayed type hypersensitivity response [47,77–79].

There is evidence that exercise may be particularly beneficial in frail elderly and those with impaired immune functioning [80]. A 17-week progressive exercise intervention (RCT; aerobic exercise, skill training, and games, 45 min/session, 2×/week) in 112 frail elderly men and women (mean age, 79), along with a nutrition intervention (enriched foods) had a small beneficial effect on delayed type hypersensitivity responsiveness, an *in vivo* measure of cellular immune response [80]. In 29 previously sedentary elderly, Woods et al found 6 months of aerobic training (60% VO_{2max} , 40 min/session, 3×/week) induced slight increases in T cell proliferation in response to mitogenic stimulation and in basal natural killer cell cytotoxic activity [81]. Overall, the small changes seen in some prospective studies generally fail to support immune benefits suggested by cross-sectional studies. However, critics caution that prospective studies have been limited in duration and statistical power and often fail to examine clinically relevant *in vivo* measurements of immune response [82]. More research is needed to define and describe potential immune benefits of long-term training in both healthy and impaired seniors.

Role of Exercise in Prevention and Treatment of Chronic Disease

CHD

Cardiac rehabilitation and exercise training are associated with improved outcomes in the elderly. The beneficial effects of endurance (aerobic) exercise on lipoprotein profiles and cardiovascular health were discussed previously. In CHD rehabilitation, strength training complements an aerobic exercise prescription [83–86]. While aerobic training more effectively modifies cardiovascular risk factors associated with the development of coronary artery disease, resistance training offers greater development of muscle strength, endurance, and mass [87]. PRT can decrease myocardial demands during daily activities, such as carrying groceries or lifting objects. A series of cross-sectional and cohort studies have shown that exercise training, when initiated early after hospitalization, can result in a 10% to 60% increase in functional capacity and a 10% to 25% reduction in myocar-

dial work at standardized exercise workloads [88–91]. The extent of cardiovascular disease in a patient will determine the level of supervision and monitoring necessary for safe and effective training.

Hypertension

Chronic hypertension is a major risk factor for CHD and is estimated to be involved in nearly 70% of all stroke cases [92,93]. Current National Heart, Lung, and Blood Institute recommendations address the importance of strict hypertension control as early as the prehypertension stage and promote lifestyle modification and as an integral treatment step enhancing pharmacologic options [93]. Dietary changes, including the DASH diet (Dietary Approaches to Stop Hypertension), are recommended, along with regular aerobic activity at least 30 minutes per day most days of the week [93]. Moderate-intensity aerobic exercise (55%–70% maximal heart rate or 40%–60% VO_{2max}) has repeatedly been shown to reduce blood pressure (BP) in patients with mild to moderate hypertension [94–97]. Studies indicate that endurance exercise training will elicit an average reduction of 10 mm Hg in both systolic and diastolic BPs in individuals with mild hypertension (systolic BP 90–140 mm Hg, diastolic BP 105–180 mm Hg) [94]. A meta-analysis of recent trials in hypertensive patients suggests that reductions in systolic BP as small as 1 to 3 mm Hg decrease the relative risk of stroke by as much as 20% to 30% [98].

Of specific relevance to the aging population, 9 months of low- or moderate-intensity aerobic training (53% and 73% VO_{2max} , respectively) was shown to decrease BP in hypertensive men and women aged 60 to 69 in a longitudinal study [99]. Interestingly, low-intensity training may lower BP as much or more than moderate-intensity training in older persons with hypertension. Strength training also was shown to reduce resting BP in 21 men and women aged 65–73 in a 6-month prospective intervention [100]. According to the latest guidelines from the Joint National Committee for the Detection, Evaluation, and Treatment of Hypertension, the changes in resting BP noted in older adults after 6 months of heavy strength training represent a shift from the high normal to the normal category. Endurance exercise coupled with PRT offers a nonpharmacologic alternative to reduce hypertension incidence and severity in susceptible individuals.

Congestive Heart Failure

The ability of congestive heart failure (CHF) patients to comfortably perform activities of daily living can be enhanced through exercise. Improvements in exercise duration and VO_{2max} have been demonstrated in many RCTs (for more complete reviews, see Piña et al [101] and Witham et al [102]). Changes in peak VO_2 from 12% to 31% generally occur

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quickly (by the third week of training) and persist with continued exercise compliance. In older women (aged ≥ 65) with CHF, 10 weeks of PRT (80% 1-RM, 3 \times /week) was shown to counteract the skeletal muscle myopathy of heart failure and improve muscle strength, endurance, and type I muscle fiber area [103]. While a few studies have reported exercise-related complications that highlight the need for medical supervision and/or educated self-monitoring, the majority of researchers have found no exercise-related complications with low- to moderate-intensity exercise training (35% to 70% maximal heart rate, 20%–60% $\text{VO}_{2\text{max}}$) in CHF patients.

Many potential mechanisms exist for this improvement in oxidative metabolism and exercise tolerance in CHF patients, including decreased catecholamine levels, increased ventilatory capacity through respiratory muscle conditioning, delayed blood lactate accumulation, improved endothelial function, myocardial adaptations, and modification of skeletal muscle morphology. Santoro et al reported the average size of the mitochondria in 6 heart failure patients increased by 23.4% after 16 weeks of supervised upper and lower extremity exercise training [104]. While large-scale, randomized trials indicating direct improvements in survival and quality of life are limited, preliminary results are promising and indicate that exercise may offer a benefit for individuals with stable CHF.

Diabetes

Results from the Diabetes Prevention Program, a 27-center RCT ($n = 3234$), suggest that diet and exercise can be more effective than pharmacologic therapy (metformin) in preventing or delaying the onset of type 2 diabetes in people with impaired glucose tolerance [105–107]. A lifestyle intervention designed to achieve and maintain a weight reduction of at least 7% of initial body weight through a low-calorie, low-fat diet and moderate physical activity (such as brisk walking) for 150 min/week or more decreased diabetes incidence by 58%, while metformin reduced the incidence by only 31%. Effects were similar in men and women and in all racial and ethnic groups, with the most profound impact in the oldest subgroup (aged ≥ 60). These results complement earlier findings and demonstrate the efficacy of diabetes prevention in high-risk subjects through diet and exercise interventions [108]. Exercise can decrease the risk of CHD in diabetics through improved cardiovascular fitness and lipoprotein risk profile and reduced blood pressure and central obesity.

In type 2 diabetic patients, exercise may improve glucose uptake and insulin sensitivity and return elevated blood glucose to normal levels. Animal studies indicate this effect may be mediated by increases in the GLUT-4 glucose transporter protein in muscle [109]. Clinical studies confirm these results and suggest that older human skeletal muscle retains the ability to increase muscle GLUT-4 and improve insulin action in

response to endurance training [110]. Further, exercise can improve modifiable risk factors for the premature coronary disease associated with diabetes. Evidence for an exercise training benefit is strongest for improvements in endothelial vasodilator function and left ventricular diastolic function, with fewer studies examining improvements in arterial stiffness and systemic inflammation [111]. While most studies demonstrating the beneficial effects of exercise in diabetics have used an aerobic exercise intervention, Castaneda and colleagues demonstrated 16 weeks of supervised PRT (60% to 80% 1-RM, 45 min/session, 3 \times /week) can improve glycemic control and reverse some abnormalities associated with the metabolic syndrome in older Latino adults with type 2 diabetes (RCT; $n = 62$; mean age, 66) [112]. Program compliance was high. Decreased plasma glycosylated hemoglobin, systolic BP, and trunk fat mass, increased lean mass, and a reduction in prescribed diabetes medication doses were evident. Since muscle tissue represents the primary site for glucose storage and oxidation, increased lean mass results in greater capacity for glucose disposal, and thereby improved glycemic control in type 2 diabetics. Exercise of any intensity level can be used to modify morbidity and mortality risk factors in patients with type 1 diabetes provided they have good blood glucose control prior to initiating the exercise program and adequate knowledge of the use of carbohydrate supplementation and insulin therapy to maintain blood glucose levels throughout each exercise session [113].

Arthritis

Osteoarthritis (OA), a painful and disabling disease, is strongly associated with aging. Evidence from large RCTs indicates that both aerobic training and PRT can reduce pain and improve function in patients with knee OA [114–116]. A daily walking program was shown in an RCT to be effective in addressing symptoms of OA [117]. Exercises especially directed toward increasing the strength of the quadriceps and preserving the normal mobility of the knee are strongly recommended [114]. PRT benefits include improvements in pain and functional index, prevention of disability in activities of daily living, and prolonged functional independence in older patients with OA [118]. For an extensive review of exercise in the management of osteoarthritis and practical recommendations for the clinician, see the 2001 report from the American Geriatrics Society Panel on Exercise and Osteoarthritis [119].

Exercise also may benefit patients with rheumatoid arthritis. In a recent meta-analysis of RCTs, the authors concluded that dynamic exercise therapy is effective in increasing aerobic capacity and muscle strength with no detrimental effects on disease activity or pain [120]. In 30 elderly patients with well-controlled rheumatoid arthritis, PRT (12 weeks, 80% 1-RM, 2 \times /week) was shown to increase strength, balance, and gait speed while reducing protein catabolism and

self-reported pain and fatigue [121,122]. Further, high-intensity training was shown to have no adverse affect on immune function in this population, alleviating the concern that exercise could further aggravate autoimmune responses [47].

Osteoporosis

Long-term, high-intensity strength training (5 exercises at 80% 1-RM, 2×/week for 1 year) has been shown to maintain and increase bone density in postmenopausal women (RCT, $n = 39$) [123]. On the other hand, short-term moderate-intensity physical activity (combined, varied exercise program with increasing intensity, 45 min/session, 2×/week for 17 weeks) was not shown to have an effect on bone parameters beyond the effect of increased consumption of nutrient-dense foods (RCT, $n = 143$) [124]. This suggests longer intervention time is required for measurable bone density improvements. Several recent meta-analyses including men and postmenopausal women demonstrate that aerobic exercise and PRT can be equally efficacious in preserving and improving bone mineral density compared with sedentary controls [125–128].

In addition to preserving lean body mass in frail elderly subjects, 17 weeks of exercise (a varied exercise program with increasing intensity, 45 min/session, 2×/week) served to significantly increase energy intake (RCT, $n = 159$) [129]. This effect is not consistent across all studies but does suggest that exercise may have the potential to affect dietary intake and thus improve micronutrient intake in elderly populations. While the effects of exercise on appetite and bone density are still under investigation, it is clear that high-intensity PRT can help prevent falls independent of bone parameters [130].

Obesity

More than 60% of the U.S. adult population is overweight or obese, a condition that increases the risk of several chronic diseases, including CHD, stroke, type 2 diabetes, hypertension, and cancers at multiple sites [131,132]. Investigators conducting a large prospective cohort study recently estimated that current patterns of overweight and obesity in the United States could account for 14% of all deaths due to cancer in men and 20% of those in women [133]. An RCT on the impact of exercise on total and intra-abdominal body fat in 173 overweight and obese postmenopausal women found that regular moderate-intensity exercise (3.5 ± 1.2 days/week, 176 ± 91 min/week), such as brisk walking or bicycling, resulted in reduced body weight and fat [134]. The changes seen in this study were dose-dependent, with more active exercisers losing more intra-abdominal fat. A total body strength training program also was shown to decrease intra-abdominal fat and increase strength in 14 healthy older women (mean age, 67 ± 1), although this study lacked a

control group for comparison [135]. PRT has the additional advantage of preventing the concomitant loss of bone and muscle seen with dieting alone or dieting plus aerobic exercise [136]. While both aerobic and PRT programs have been used successfully to address overweight and obesity [137], a mixed program incorporating endurance and strength training combined with diet and lifestyle changes may offer the best means for weight loss and weight maintenance at a lower weight.

Conclusion

In both aging and disease, inactivity is associated with physical and functional decline. A substantial body of literature clearly demonstrates the health benefits of physical activity and exercise training at all life stages. Exercise also can contribute to better nutritional status by increasing energy requirements (which may prevent protein and micronutrient deficiencies), improving dietary protein retention, and attenuating the age-related drop in resting energy expenditure. Physicians can help patients by explaining the benefits of exercise and encouraging sound and effective changes in physical activity levels. While care needs to be taken when starting a previously sedentary individual on an exercise regimen, inactivity presents a far greater danger than the possibility of injury from exercise. While some patients will have musculoskeletal complaints when starting a new program [138], the frequency of injury from moderate-intensity exercise has been shown repeatedly to be very low, even in elderly populations with chronic disease [139–144]. Often, minor modifications to an existing exercise program, such as increasing warm-up and cool-down periods or decreasing exercise intensity, can decrease muscle soreness and risk of injury and increase long-term adherence. Exercise is an invaluable prescription in efforts to prevent disease, treat chronic diseases, and maintain functional capacity and independence in our aging population.

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